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| PERKINS COIE LLP P.O. BOX 2168 MENLO PARK, CA 94026 | | | SCHNIZER, RICHARD A | |
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1635

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/603,385

Applicant(s)

ZHANG, FEN

Examiner

Richard Schnizer, Ph. D

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,7,10,12,13,15,16 and 20-24 is/are pending in the application.
- 4a) Of the above claim(s) 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1,7,10,12,15,16 and 20-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/24/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

An amendment was received and entered on 2/9/06.

Claims 2-6, 8, 9, 14, and 17-19 were canceled and claims 21-24 were added as requested.

Claims 1, 7, 10, 12, 13, 15, 16, and 20-24 remain pending.

The elected invention of "growth factors" and "amniotic membrane" is under consideration in this Office Action, so claim 13 is withdrawn pursuant to 37 CFR 1.142(b) because it is drawn to a nonelected species, there being no allowable generic or linking claim. In a telephone interview on 6/28/04, Applicant elected the species "growth factors" and "amniotic membrane" with traverse. Subsequent to the first Office Action on the merits, Applicant filed a reply on 11/24/04 in which the election was confirmed by no reasons for traverse were given. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)) and is made FINAL.

Priority

Priority is claimed in the first line of the specification to provisional application 60/391,550, filed 6/24/2002. The effective filing date of the application is considered to be 6/24/2002.

Rejections Withdrawn

The rejection of claims 16, and 20 under 35 U.S.C. 112, first paragraph is withdrawn after further consideration.

The rejection of claims 1, 7, 10, 12, 16, and 20 under 35 U.S.C. 102(b) as being anticipated by Faulk et al (Lancet 1(8179): 1156-1158, 1980) as evidenced by Uchida et al (J. Neurosci. Res. 62: 585-590, 2000) is withdrawn in view of Applicant's amendment requiring transformation of the amniotic epithelial cells with one or more recombinant expression vectors.

The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by Eming et al (Biotech. Bioeng. 52(1): 15-23, 1996) is withdrawn in view of Applicant's amendment requiring amniotic epithelial cells.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 10, 12, 15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7, 10, 12, 15 are indefinite because they recite said cells without proper antecedent basis in each of the last two clauses of claim 1. Insertion of "transformed" immediately before "cells" is suggested.

It is also unclear what is meant by "said contact the skin wound for expression of the bioactive protein for treating the skin wound" because it is unclear what is required for treating the skin wound. Is contact by the cells sufficient to meet the claim requirements, or must the bioactive protein be one that is capable of treating the skin wound?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1, 7, 10, and 12 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating a skin wound comprising delivering a growth factor to a wound in the skin of a patient by administering to the wound site amniotic epithelial cells that secrete the growth factor, does not reasonably provide enablement for treating skin wounds by expression of bioactive proteins other than secreted growth factors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to methods and compositions for treating a skin wound by administering topically to the wound amniotic epithelial cells supported on a membrane, wherein said cells have been transformed with one or more recombinant expression vectors encoding any bioactive protein. The claims require that the transfected cells

“contact the skin wound for expression of the bioactive protein for treating the skin wound.” In one interpretation, the claims require that the bioactive protein must be one that is capable of treating the skin wound. The only type of protein that the specification enables the use of is a growth factor.

The specification provides no working example of treating a skin wound through the use of amniotic epithelial cells. The specification discloses the expression of secretable proteins such as growth factors, but does not disclose expression of any bioactive protein that is not secreted, nor does it disclose what kind of non-secreted bioactive protein would be useful for wound treatment. The specification envisions the expression of growth factors, anti-microbial proteins, anti-inflammatory proteins, protease inhibitors, and hair growth proteins. No guidance is presented as to how to deliver any type of molecule other than a secretable gene product. No guidance is presented with regard to how many amniotic epithelial cells must be transfected with what type of expression construct to achieve the appropriate level of expression of any specific gene product for any specific desired effect. Instead the specification teaches a working example in which an amniotic membrane is stripped of its epithelium, reconstituted with Madin-Darby Canine Kidney (MDCK) cells that stably express PDGF-beta, and applied to a rabbit chronic wound model. Accelerated healing is reported.

The full scope of the claims relating to wound healing by delivery of genetically modified cells that express any bioactive protein is not fully enabled due to a lack of guidance. This art was recognized as highly unpredictable at the time of filing, and the

specification fails to provide the guidance that is missing from the prior art. At the time the invention was made, successful implementation of gene therapy protocols was not routinely obtainable by those skilled in the art. Verma et al (Nature 389: 239-242, 1997) teach that "there is still no single outcome that we can point to as a success story (p. 239, col 1). The authors state further, "Thus far, the problem has been the inability to deliver genes efficiently and to obtain sustained expression" (p.239, col. 3). With specific regard to ex vivo therapy using retroviral vectors, Verma taught that expression of transgenes was shut off within five to seven days, even in animals lacking a functional immune system. Verma also points out that the search for an appropriate enhancer-promoter combination is a case of trial and error for each given type of cell. See page 240, column 2, lines 10-1, and sentence bridging columns 2 and 3. Anderson (Nature 392:25-30, 1998) confirms the unpredictable state of the art, stating that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease" (p. 25, col. 1) and concluding, "Several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered" (p.30). More recently, Romano et al (2000) reviewed the general state of gene therapy, and found that the problems relating to gene delivery and expression discussed above persisted. See entire document, especially, last sentence of abstract; last sentence of column 1 on page 20 to column 2, line 6; page 21, column 1, lines 1-9 and 18-21; sentence bridging columns 1 and 2 on page 21; and first sentence of last paragraph on page 21.

The prior art taught that wound healing may be facilitated by the delivery to a wound of expression vectors encoding growth factors. See e.g. US Patent 5962427, claims 1-14, and especially claims 6-11. Furthermore, the prior art taught that epithelial cells may be transfected with expression vectors encoding growth factors, applied to a membrane, and administered to a wound to improve healing. For example, Eming (Invest. Dermatol. 105(6): 756-763, 1995) taught that grafts of keratinocyte monolayers retrovirally modified to overexpress PDGF-A aided in tissue regeneration when administered to the skin of immunodeficient (athymic) mice. See abstract, and page 757, column 2, fourth full paragraph. These results were reproduced by Eming et al (Biotech. Bioeng. 52: 15-23, 1996), see abstract and page 19, column 1, first full paragraph, and column 2, first full paragraph. As a result methods of improving wound healing by administration of epithelial cells modified to express growth factors is considered to be enabled.

However, the specification does not enable the treatment of wounds by delivery of molecules other than growth factors, as there is no guidance whatsoever as to how to use amniotic epithelial cells to treat wounds by expression of any other type of protein. Wound healing is recognized as a very complex process involving intricate interactions between a variety of cell types, structural proteins, growth factors, and proteinases. (Stadelmann, W.K., et al., Am J Surg 176(Supp 2A):26S-38S, (1998)). Some of the factors involved in wound healing may affect more than one aspect of the process. So, when a therapeutic regime is contemplated for impaired wound healing, the various process involved in wound healing, i.e. inflammation, angiogenesis, mesenchymal cell

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chemotaxis and proliferation, epithelialization, wound contraction, collagen synthesis, and remodeling, must be critically considered, and an accurate diagnosis of the factors impairing wound healing must be made. See Eming et al (Cells, Tissues, Organs (2002) 172(2): 105-117) page 106, column 2, first full paragraph. The specification provides no guidance as to the appropriate level of expression of any gene product, nor how to obtain and limit expression within such limits. For example, although the specification suggests the use of anti-inflammatory proteins, it provides no guidance as to how much expression of any anti-inflammatory protein is therapeutic. This is a critical omission in view of the fact that it is recognized in the specification and the prior art that inflammation is a normal part of wound healing. Indeed, Eming (2002) taught that impairment of inflammation could cause inadequate angiogenesis, mesenchymal cell chemotaxis and proliferation, epithelialization, wound contraction, collagen synthesis, and remodeling. It follows that overexpression of anti-inflammatories could actually impede wound healing.

The high degree of unpredictability associated with the claimed method underscores the need to provide teachings in the specification that would provide the artisan with specific treatment regimens that achieve wound healing with bioactive proteins other than growth factors. However, the specification does not provide such guidance and fails to provide any correlation between vectors, cells comprising vectors, dosage amounts, therapeutic genes other than growth factor genes, and any specific disease or condition treatable by the nucleic acids or cells comprising such as disclosed in the instant specification. Without such guidance in the specification and the lack of

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correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

Response to Arguments

Applicant's arguments filed 2/9/06 have been fully considered but they are not persuasive. At pages 7 and 8 of the response Applicant asserts that the specification teaches how to transfect amniotic epithelial cells, how to express bioactive proteins, and how to prepare vectors. Applicant also asserts that expression of the encoded protein upon topical administration of the cells to the wound is expected and predictable. However, this portion of the rejection set forth previously regarding the scope of bioactive proteins that are not growth factors. Because this is not addressed the arguments are unpersuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 7, 10, 12, 15, 16, 20, 21, and 23, are rejected under 35 U.S.C. 103(a) as being unpatentable over Faulk et al (Lancet 1(8179): 1156-1158, 1980), in view of

Eming et al (Biotech. Bioeng. 52(1): 15-23, 1996) and Sakuragawa (US Patent 6117676, issued 9/12/00).

Faulk taught a method of treating wounded skin by topical application of amniotic basement membrane comprising human amniotic epithelial cells. See abstract, and page 1156, column 2, first two paragraphs.

Faulk did not teach amniotic epithelial cells transformed with one or more recombinant expression vectors encoding a bioactive protein.

Eming taught a method of promoting growth and vascularization in a wound by delivering PDGF-A to a patient. Epithelial keratinocytes were genetically modified with a retrovirus to express PDGF-A, and were attached to a supporting membrane and administered to the skin of an immunodeficient (athymic) patient, resulting in improved growth and vascularization in the wound. See abstract, and page 17, column 1, second paragraph under the heading "Grafting". Eming's goal was to enhance the function of cells used in skin substitutes by genetic modification to produce a cell-based vehicle for the local synthesis and delivery of wound-healing growth factors.

Sakuragawa taught that amniotic epithelial cells could be transfected by either plasmid or adenoviral vectors, and that amniotic epithelial cells do not express HLA-A, B, C and DR antigens and do not cause rejection reactions or topical inflammation even when transplanted allogeneically. See column 2, lines 9-13 and 27-39; column 3, lines 51-67; column 4, lines 1-16 and 25-35; and column 5, line 25 to column 6, line 17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Faulk by transfecting the amniotic epithelial cells with

the vector of Eming. One would have been motivated to do so because Eming shows that delivery of PDGF-A by transfected epithelial cells attached to a membrane results in tissue regeneration. One would have selected amniotic epithelial cells because Sakuragawa teaches that these cells can be conveniently transplanted allogeneically without rejection due to the absence of cell surface HLA class II antigens, and a much diminished amount of HLA class I antigens, and because it was routine in the art at the time of the invention to apply to wounds such as ulcers amniotic membranes comprising amniotic epithelial cells. This would allow study of the healing process in immune-competent animals without instigation of inflammation beyond that which is ordinarily associated with wound healing. Also, Sakuragawa demonstrates that these cells can be transfected by means of viruses or plasmids, and suggests their use in therapeutic applications involving administration of the cells to skin. Finally, using cells on an amniotic membrane, as taught by Faulk, eliminates the step of applying cells to a synthetic membrane, thereby simplifying the procedure of Eming.

Thus the invention as a whole was prima facie obvious.

Claims 1, 7, 10, 12, 15, 16, 20, 21, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Faulk et al (Lancet 1(8179): 1156-1158, 1980), in view of Eming et al (Biotech. Bioeng. 52(1): 15-23, 1996), Sakuragawa (US Patent 6117676, issued 9/12/00), and Pollock et al (US Patent 6191269, issued 2/20/2001).

The teachings of Faulk, Eming, and Sakuragawa are discussed above and can be combined to render obvious methods and compositions for delivering molecules to a

patient by genetically modifying amniotic epithelial cells to produce the molecule, and administering the amniotic epithelial cells on an amniotic membrane. These references teach the use of retroviral, plasmid, and adenoviral vectors for transfection of epithelial cells.

These references do not teach the use lentiviral vectors, adeno-associated virus, or cosmid vectors to transfect cells.

Pollock taught that plasmids, cosmids, retroviral vectors, lentiviral vectors, adenoviral vectors, and adeno-associated viral vectors could be used interchangeably as expression vectors in eukaryotic cells. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). As such, it would have been obvious to substitute lentiviral, adeno-associated virus, or cosmid vectors for the retroviral, plasmid, or adenoviral vectors of Eming and Sakuragawa.

Thus the invention as a whole was prima facie obvious.

Claims 1, 7, 10, 12, 15, 16, and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein et al (US Published Application 2003/0091543) in view of Sakuragawa (Cell Transplantation 4(3): 343-346, 1995) taken with the evidence of Marshall (US Patent 6479052).

This rejection is directed to a generic embodiment of the rejection which does not require an amniotic membrane. See claim 12, which recites a matrix.

Klein taught a method of modulating the delivery of a growth factor to an animal by topically delivering to a skin wound a graft comprising a membrane comprising a biocompatible matrix comprising amniotic membrane cells genetically modified to express a growth factor. See e.g. claims 4, 8, and 21, and paragraphs 13 and 63. The method can be used to treat abnormal wound healing. See e.g. claim 31. Klein taught that one matrix that could be used to for grafts applied to the skin was INTEGRA, a collagen glycosaminoglycan matrix. Marshall (US Patent 6479052) disclosed at column 7, lines 19-22 that INTEGRA is a membrane. Klein suggested that cells be genetically modified by transfection with plasmid, retroviral, adeno-associated virus, or adenoviral vectors encoding the growth factor. See paragraphs 29, 72, and 86. Growth factors for expression included vascular endothelial cell growth factors, platelet derived growth factors, epidermal growth factors, fibroblast growth factors, hepatocyte growth factors, insulin-like growth factors, and transforming growth factors, human growth hormone, insulin-like growth factor, and others. See paragraph 48 and claim 8.

Although Klein taught the use of amniotic cells generally, Klein did not explicitly teach the use of amniotic epithelial cells specifically.

Sakuragawa taught that human amniotic epithelial cells could be transfected by either plasmid or adenoviral vectors, and that amniotic epithelial cells do not express HLA-A, B, C and DR antigens and do not cause rejection reactions or topical inflammation even when transplanted allogeneically. See e.g. claim 2, column 2, lines

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9-13 and 27-39; column 3, lines 51-67; column 4, lines 1-16 and 25-35; and column 5, line 25 to column 6, line 17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use amniotic epithelial cells in the invention of Klein for at least two reasons. First, Klein teaches the use of amniotic cells generally, but does not teach the removal of amniotic epithelial cells from non-epithelial amniotic cells. As a result, transfection of the amniotic cells as a group would result in transfection of the amniotic epithelial cells. Second, one would have been motivated to use the epithelial cells in particular because Sakuragawa exemplified their use for expression and delivery of exogenous gene products and taught that they do not express HLA-A, B, C and DR antigens and do not cause rejection reactions or topical inflammation even when transplanted allogeneically.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 2/9/06 have been fully considered but they are not persuasive.

Applicant addresses the obviousness rejections at pages 12-14 of the response. Applicant asserts that modification of Faulk et al "to use transfected amnion epithelial cells would necessarily require harvesting the cells, transfecting the cells, culturing the transfected cells, selection of the transfected cells, etc., a process that destroys the natural angiogenic factors sought in the therapy described by Faulk et al." this is

unpersuasive because Applicant presents no evidence that the process cited above “destroys the natural angiogenic factors sought in the therapy described by Faulk”. This appears to be merely a statement of opinion. Further, Applicant presents no evidence that one of ordinary skill in the art could not transfect the cells of Faulk on the membrane, without isolation, amplification, and selection. Applicant asserts that nothing in the cited art provides an expectation of success for treating skin wounds with transfected cells topically applied on a support. This is unpersuasive because Applicant has presented no evidence to suggest that there would be no reasonable expectation of success based on the cited art. Faulk taught that therapy could be obtained with non-transfected amniotic epithelial cells on a membrane support. Applicant has presented no evidence that transfecting these cells would in any way decrease the therapeutic effect demonstrated by Faulk. Applicant has presented no reason why one of ordinary skill in the art would not expect to be able to transfect amniotic epithelial cells either in suspension or attached to a membrane. The evidence of record (Sakuragawa) indicates that amniotic epithelial cells can be transfected, and there is no evidence of record that indicates any unpredictability regarding the ability to transfect these cells on a membrane, or to culture suspension-transfected epithelial cells and reattach them to a membrane as taught by Eming.

Regarding the rejection over Klein, Sakuragawa, and Marshall, Applicant argues that nothing in any of the references would lead one skilled in the art to pick amniotic epithelial cell of Sakuragawa and place it on a biocompatible membrane as in Klein. This is unpersuasive. As stated in the rejection, one would have been motivated to use

amniotic epithelial cells because Sakuragawa exemplified their use for expression and delivery of exogenous gene products, and taught that they do not express HLA-A, B, C and DR antigens and do not cause rejection reactions or topical inflammation even when transplanted allogeneically. Applicant addressed these reasons for motivation only by asserting that "there is nothing to show or suggest that modified amniotic epithelial cells could be grown in such a way for administration on a support matrix." This is unpersuasive because Applicant has presented no evidence that this would be unpredictable, or that one of ordinary skill in the art would not reasonably expect to be able to do so.

For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'RS', with a long horizontal line extending to the right.

Richard Schnizer, Ph.D.
Primary Examiner
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